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 SAHIN, Ugur
 HELFTENBEIN, Gerd
 SCHLÜTER, Volker

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- <141> 2006-03-24
- <150> PCT/EP2004/010697
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1635

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Lys Asp Phe Asp Cys Asn Thr Arg Gln Pro Gly Cys Ser Asn Val Cys 50 60

Phe Asp Glu Phe Phe Pro Val Ser His Val Arg Leu Trp Ala Leu Gln 65 70 75 80

Leu Ile Leu Val Thr Cys Pro Ser Leu Leu Val Val Met His Val Ala 85 90 95

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Trp	Thr 130	Tyr	Val	Cys	Ser	Leu 135	Val	Phe	Lys	Ala	Ser 140	Val	Asp	Ile	Ala
Phe 145	Leu	Tyr	Val	Phe	His 150	Ser	Phe	Tyr	Pro	Lys 155	Tyr	Ile	Leu	Pro	Pro 160
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Thr	Ala	Ala 195	Ile	Суѕ	Ile	Leu	Leu 200	Asn	Leu	Val	Glu	Leu 205	Ile	Tyr	Leu
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His Cys Pro Ser Ala Gly Thr Lys Cys Leu Val Ser Gly Trp Gly Thr 180 185 190

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Leu Ser Phe Ala Cys Pro Gly Gly Arg Tyr Ala Gly Ser Arg Pro Ala 50 55 60

Pro Val Ala Gly Met Asp Arg Asp Gln Gln Arg Ala Glu Ser Ala Cys 65 70 75 80

Val Pro His Ser Arg Ser Arg Gly Pro Asn Leu Pro Ser Ala Gln Ser 85 90 95

Pro Ala Gln Ser Leu Pro Gly Pro Glu Leu Ser Gln Thr Pro His Pro 100 105 110

His Ser Arg Leu Thr Pro Arg Ser Trp Ala Trp Ala Pro Leu Ala Arg 115 120 125

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Thr Arg Arg His Leu Phe Ser Glu Ala Ala Leu Pro Pro Tyr Arg Leu 20 25 30

Ser Gln Gly His Phe Leu Thr Ala Leu Gly Gly Leu Met Ala Val Pro 35 40 45

Phe Ile Leu Ala Lys Asp Leu Cys Leu Gln Gln Asp Pro Leu Thr Gln 50 55 60

Ser Tyr Leu Ile Ser Thr Ile Phe Phe Ala Pro Ala Ser Ala Cys Ser 65 70 75 80

Cys Lys Leu Pro Ile Pro Gln Gly Gly Thr Phe Ala Phe Val Val Ile 85 90 95

Ser Leu Ala Met Leu Ser Leu Pro Ser Trp Asn Cys Pro Glu Trp Thr 100 105 110

Leu Ser Ala Ser Gln Val Asn Thr Asn Phe Pro Glu Phe Thr Gln Lys
115 120 125

Trp Gln Lys Arg Ile Gln Glu Gly Ala Ile Met Val Thr Ser Cys Val Arg Met Leu Val Gly Phe Ser Gly Leu Thr Gly Phe Leu Met Gly Phe Ile Cys Ser Leu Ala Val Ala Pro Thr Asn Cys Leu Val Ala Leu Pro Leu Leu Asp Ser Ala Gly Asn Asn Ala Gly Ile Gln Trp Gly Ile Ser Ala Met Tyr Cys Phe Val Leu Arg Leu Arg Lys Asp Glu Leu Trp Pro Phe Gly Ser Pro Arg Leu Arg Leu Pro Pro Ser Pro Pro Arg Asp Arg 215 Arg His Val Pro Thr Pro Val Ile Gly Gly Met Thr Leu Phe Gly Val 230 Ile Thr Ala Val Gly Ile Ser Asn Leu Gln Tyr Val Asp Met Asn Leu Ser Arg Ser Leu Phe Ala Phe Gly Phe Ser Ile Tyr Cys Gly Leu Thr Ile Pro Asn Arg Val Ser Lys Asn Pro Glu Met Leu Gln Thr Gly Ile 280 Leu Gln Pro Asp Gln Val Val Gln Met Leu Leu Thr Met Gly Met Phe 295 Ile Ser Gly Phe Leu Gly Phe Leu Leu Asp Asn Thr Ile Pro Glu Leu 310 Leu Gln <210> 39 <211> 20 <212> DNA <213> Artificial Sequence <220> <223> Oligonucleotide <400> 39

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Tyr Arg Ile Ala Arg Arg Met Lys Pro Thr His Thr Met Val Asn Cys 35 40 45

Trp Phe Cys Asn Gln Asp Thr Leu Val Pro Tyr Gly Asn Arg Asn Cys 50 60

Trp Asp Cys Pro His Cys Glu Gln Tyr Asn Gly Phe Gln Glu Asn Gly 65 70 75 80

Asp Tyr Asn Lys Pro Ile Pro Ala Gln Tyr Leu Glu His Leu Asn His 85 90 95

Val Val Ser Ser Ala Pro Ser Leu Arg Asp Pro Ser Gln Pro Gln Gln
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Trp Val Ser Ser Gln Val Leu Leu Cys Lys Arg Cys Asn His His Gln
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Thr Thr Lys Ile Lys Gln Leu Ala Ala Phe Ala Pro Arg Glu Glu Gly 130 135 140

Arg Tyr Asp Glu Glu Val Glu Val Tyr Arg His His Leu Glu Gln Met 145 150 155 160

Tyr Lys Leu Cys Arg Pro Cys Gln Ala Ala Val Glu Tyr Tyr Ile Lys 165 170 175 His Gln Asn Arg Gln Leu Arg Ala Leu Leu Leu Ser His Gln Phe Lys 180 185 190

Arg Arg Glu Ala Asp Gln Thr His Ala Gln Asn Phe Ser Ser Ala Val 195 200 205

Lys Ser Pro Val Gln Val Ile Leu Leu Arg Ala Leu Ala Phe Leu Ala 210 215 220

Cys Ala Phe Leu Leu Thr Thr Ala Leu Tyr Gly Ala Ser Gly His Phe 225 230 235 240

Ala Pro Gly Thr Thr Val Pro Leu Ala Leu Pro Pro Gly Gly Asn Gly 245 250 255

Ser Ala Thr Pro Asp Asn Gly Thr Thr Pro Gly Ala Glu Gly Trp Arg
260 265 270

Gln Leu Leu Gly Leu Leu Pro Glu His Met Ala Glu Lys Leu Cys Glu 275 280 285

Ala Trp Ala Phe Gly Gln Ser His Gln Thr Gly Val Val Ala Leu Gly 290 295 300

Leu Leu Thr Cys Leu Leu Ala Met Leu Leu Ala Gly Arg Ile Arg Leu 305 310 315 320

Arg Arg Ile Asp Ala Phe Cys Thr Cys Leu Trp Ala Leu Leu Gly 325 330 335

Leu His Leu Ala Glu Gln His Leu Gln Ala Ala Ser Pro Ser Trp Leu 340 345 350

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Glu Ala Tyr Ala Leu Pro Leu Val Val Lys Val Val Asp Asn Trp Ala

Phe Gly Gln Gln Thr Val Thr Gly Gln Ala Asn Ile Asp Phe Leu Gln

Pro Tyr Phe Cys Asp Pro Trp Ala Gln Asp Tyr Met His Pro Lys Leu

Pro Thr Leu Ser Glu Lys Lys His Gln Asp Phe Leu Gly Tyr Leu Tyr 105

Arg Lys Phe Trp Phe Lys Ser Ser Lys Ala Glu Asp Glu Tyr Glu His

Glu Val Asp Trp Trp Ser Lys Leu Phe Trp Ala Thr Asp Glu His Lys 135

Ser Leu Lys Tyr Lys Tyr Lys Asp Tyr His Thr Leu Lys Val Tyr Glu

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Gln Thr Phe Lys Leu Tyr Gln Glu Gln Pro Lys Leu Asp Ser Pro Val

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435 440 445

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680

675

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Page 81

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Page 86

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- Thr Gln Leu Ala Gly Pro Ser Ser Ala Thr Cys Glu Ser Gly Ala Gly 835 840 845
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Lys Met Asn Thr Asp Asp Leu Glu Asn Ser Ser Val Thr Ser Lys Gln 55

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Pro Ser Ala Thr Ser Leu Asn Lys Ala Phe Ser Ile Asn Lys Glu Thr

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Page 99

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Val Asp Leu Thr Lys Gly His Ser His Gln Arg Ala Lys Glu Ile Leu 65 70 75 80

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660

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Page 104

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Page 115

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Page 125 Tyr Ser Arg Asp Phe Ser Phe Thr Ile Val Asp Pro Val Thr Ser Pro 120 Val Leu Asn Ile Met Val Ile Gln Thr Glu Thr Asp Arg His Ile Thr Leu His Cys Leu Ser Val Asn Gly Ser Leu Pro Ile Asn Tyr Thr Phe Phe Glu Asn His Val Ala Ile Ser Pro Ala Ile Ser Lys Tyr Asp Arg 170 Glu Pro Ala Glu Phe Asn Leu Thr Lys Lys Asn Pro Gly Glu Glu Glu 185 Glu Tyr Arg Cys Glu Ala Lys Asn Arg Leu Pro Asn Tyr Ala Thr Tyr 200 Ser His Pro Val Thr Met Pro Ser Thr Gly Gly Asp Ser Cys Pro Phe Cys Leu Lys Leu Leu Pro Gly Leu Leu Leu Leu Val Val Ile Ile Leu Ile Leu Ala Phe Trp Val Leu Pro Lys Tyr Lys Thr Arg Lys

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Leu Ser Leu Thr Phe Gly Thr Ser Met Ala Cys Gly Asn Val Gly Leu 115 120 125

Arg Ala Val Pro Leu Asp Leu Ala Gln Leu Val Thr Thr Thr Pro 130 135 140

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Leu Leu Gln Glu Glu Arg Leu Asp Ala Val Thr Leu Leu Tyr Ala Thr 210 215 220

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- His Asp Pro Lys Thr Cys Ser Phe Gln Glu Gly Arg Val Lys Leu Pro 130 135 140
- Glu Asp Cys Pro Gln Leu Leu Arg Val Asp Lys Ile Leu Val Pro Val 145 150 155 160
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Ile Asn Ile Cys Glu Val Leu Asn Ala Thr Glu Met Thr Cys Gln Ala

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530

Page 138

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Arg Leu His Gln Asn Cys Ser Glu Gln Ile Lys Pro Ile Asn Asp Thr 50 55 60

His Ser Leu Asn Asp Thr Met Trp Cys Ser Trp Ala Pro Phe Asp Lys 70 75 80

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Ala Tyr Ala Ile Gly Met Phe Ile Ser Gly Val Phe Gly Glu Arg Leu 100 105 110

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35 40 45

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35 40 45

Pro Pro Glu Gly Ala Val Gly Asp Ile Cys Lys Lys Glu Asp Ala Gly 50 55 60

Asn Met Pro Ser Thr Ser Glu Gly Ser Ile Tyr Pro Glu Met Ala His 65 70 75 80

Phe Leu Arg Asn Lys Leu Ala Gly Ser Ser Val Arg Lys Pro Asp Ser 85 90 95

Gly Phe Leu Trp Glu Gly Ala Leu Arg Ala Trp Leu Phe Leu Ile Leu 100 105 110

Ile Val Leu Thr His Ile Met Trp Val Pro Leu Val Gln Val Ser Pro 115 120 125

Asn Ala Pro Leu Phe His Tyr Ile Glu Ser Ile Ala His Asp Leu Gly 130 135 140

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Arg Ile Phe Thr Pro Val Val Phe Phe Thr Thr Ala Phe Asp Met Asp 85 90 95

Thr Tyr Met Leu Gln Lys Leu Phe Trp Gln Ile Leu Leu Ile Ser Ile 100 105 110

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- Gly Met Val Lys Leu Glu Lys Ser Lys Pro Gly Leu Gly Ile Asp Gln 865 870 875 880
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Glu Gly Lys Thr Asp Tyr Tyr Ala Trp Lys His Leu Val Val Gln Asp 100 105 110

Lys Asn Lys Ser Asn Thr His Lys Tyr Arg Met Ile Ile Cys Val Ile 115 120 125

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660 665 670

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Val Lys Phe Tyr Arg Asp Gly Lys Phe Leu His Phe Ser Lys Glu Asn 65 70 75 80

Gln Thr Leu Ser Met Gly Ala Ala Thr Val Gln Ser Arg Gly Gln Tyr 85 90 95

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Pro Phe Asp Phe Lys Thr Asn Pro Ser Trp Leu Asn Ile Asn Tyr Lys 50 55 60

Val Leu Leu Val Ser Thr Glu Val Thr Tyr Phe Val Cys Gly Leu Phe 65 70 75 80

Phe Val Pro Val Val Glu Glu Trp Val Trp Asp Tyr Ala Ile Ser Val 85 90 95

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480

513

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Lys Val Trp Cys Arg Phe Leu Pro Glu Gly Cys Gln Pro Leu Val Ser 50 60

Ser Ala Val Asp Arg Arg Ala Pro Ala Gly Arg Arg Thr Phe Leu Thr 65 70 75 80

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Glu Asp Ala Gly Glu Tyr Gly Cys Met Val Asp Gly Ala Arg Gly Pro 100 105 110

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Glu Glu Thr His Lys Ile Gly Ser Leu Ala Glu Asn Ala Phe Ser Asp 130 135 140

Pro Ala Gly Ser Ala Asn Pro Leu Glu Pro Ser Gln Asp Glu Lys Ser 145 150 155 160

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<213> Homo sapiens

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Pro Glu Leu Cys Thr Phe Val Val Arg Val Leu Phe Tyr Leu Gly Pro 35 40 45

Val Tyr Leu Ala Gly Tyr Leu Gly Leu Ser Ile Thr Trp Leu Leu Leu 50 55 60

Gly Ala Leu Leu Trp Met Trp Trp Arg Arg Asn Arg Arg Gly Lys Leu 65 70 75 80

Gly Arg Leu Ala Ala Phe Glu Phe Leu Asp Asn Glu Arg Glu Phe 85 90 95

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Thr	Lys	Leu	Tyr	Phe 165	Gly	Gln	Lys	Cys	Pro 170	Arg	Val	Asn	Gly	Val 175	Lys
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Ile	Cys	Tyr 195	Ile	Gly	Asp	Cys	Glu 200	Ile	Ser	Val	Glu	Leu 205	Gln	Lys	Ile
Gln	Ala 210	Gly	Val	Asn	Gly	Ile 215	Gln	Leu	Gln	Gly	Thr 220	Leu	Arg	Val	Ile
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Val	Ser	Ile	Gly 340	Leu	Gln	His	Phe	Arg 345	Ser	Arg	Thr	Ile	Tyr 350	Arg	Asn

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<211> 294

<212> PRT

<213> Homo sapiens

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Leu Asn Glu Asp Val Asn Lys Gln Glu Glu Lys Asn Glu Asp His Thr

Pro Asn Tyr Ala Pro Ala Asn Glu Lys Asn Gly Asn Tyr Tyr Lys Asp Ile Lys Gln Tyr Val Phe Thr Thr Gln Asn Pro Asn Gly Thr Glu Ser Glu Ile Ser Val Arg Ala Thr Thr Asp Leu Asn Phe Ala Leu Lys Asn 85 Asp Lys Thr Val Asn Ala Thr Thr Tyr Glu Lys Ser Thr Ile Glu Glu 105 Glu Thr Thr Thr Ser Glu Pro Ser His Lys Asn Ile Gln Arg Ser Thr Pro Asn Val Pro Ala Phe Trp Thr Met Leu Ala Lys Ala Ile Asn Gly 135 140 Thr Ala Val Val Met Asp Asp Lys Asp Gln Leu Phe His Pro Ile Pro 150 155 Glu Ser Asp Val Asn Ala Thr Gln Gly Glu Asn Gln Pro Asp Leu Glu Asp Leu Lys Ile Lys Ile Met Leu Gly Ile Ser Leu Met Thr Leu Leu 180 185 Leu Phe Val Val Leu Leu Ala Phe Cys Ser Ala Thr Leu Tyr Lys Leu 195 200 Arg His Leu Ser Tyr Lys Ser Cys Glu Ser Gln Tyr Ser Val Asn Pro 215 Glu Leu Ala Thr Met Ser Tyr Phe His Pro Ser Glu Gly Val Ser Asp 230 Thr Ser Phe Ser Lys Ser Ala Glu Ser Ser Thr Phe Leu Gly Thr Thr 245 Ser Ser Asp Met Arg Arg Ser Gly Thr Arg Thr Ser Glu Ser Lys Ile Met Thr Asp Ile Ile Ser Ile Gly Ser Asp Asn Glu Met His Glu Asn 275 280

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45

40

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<213> Homo sapiens

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Trp Arg Val Ser Gln Arg Arg Ser Lys Thr Lys Ser Gly Pro Val Leu 35 40 45

Gly His Leu Lys Ala Met Pro Lys His Ser Val Ile Leu Gly Val His 50 55 60

Trp Lys Ala Ser Ser Tyr Pro His Thr Ser Ser Gln Ser Pro Asp Val 75 80

Asn Val Glu Ala Glu Asp His Leu Leu Leu Val Leu Leu Leu Phe Leu 85 90 95

Leu Phe Leu Phe Arg Thr Ala Thr Ile Glu Asp Leu Ala Ser His Phe 100 105 110

Pro Asp Val Phe Ser Glu Ile Leu Cys Trp Pro Ala Lys Pro Tyr Gly 115 120 125

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<213> Homo sapiens

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Arg Ser Ala Val Lys Glu Asp Glu Lys His Gly Tyr Ala Leu Leu 35 40 45

Val Pro Leu Phe Leu Tyr Leu Ile Ser Thr Ser Phe Tyr Lys Tyr Ile 50 55 60

Arg Ala Thr Leu Ser Leu Cys Ile Ser Asn Lys Ala Lys Arg Gly Cys 65 70 75 80

Asn Tyr Thr Leu Leu Gln Ser Ser Val Ser Pro Gly Asn Arg Asn Ala 85 90 95

Lys Ala Leu Lys Ala Ser Leu Phe Ala Asp Met Val Ser Trp Val Pro 100 105 110

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<213> Homo sapiens

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Phe Ala Lys Ile Phe Ile Gly Cys Leu Ala Ala Val Thr Ser Gly Met 50 55 60

Met Tyr Ala Leu Tyr Leu Ser Ala Tyr His Glu Arg Lys Phe Trp Phe 65 70 75 80

Ser Asn Arg Gln Glu Leu Glu Arg Glu Ile Thr Phe Gln Gly Asp Ser 85 90 95

Ala Ile Tyr Tyr Ser Tyr Tyr Lys Asp Met Leu Lys Ala Pro Ser Phe 100 105 110

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Lys Thr Ile Asn Ala Val Gln Gln Met Ser Leu Tyr Pro Glu Leu Ile 130 135 140

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Cys Tyr Val Thr Tyr Leu Thr Phe Ser Ala Leu Ser Ser Lys Pro Ala 65 70 75 80

Glu Val Val Leu Asp Glu His Gly Lys Asn Val Thr Ile Cys Val Pro 85 90 95

Asp Phe Gly Gln Asp Leu Tyr Arg Asp Glu Asn Leu Val Thr Ile Leu 100 105 110

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Asp Tyr Asp His Cys Arg His Leu Gln Val Pro Cys Lys Glu Leu Gln 50 55 60

Arg Val Gly Pro Ala Ala Cys Leu Cys Pro Gly Leu Ser Ser Pro Ala 65 70 75 80

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Gln Leu His Ala Val Gly Gly Val Ala Leu Thr Ser Ser His Pro Ser 50 55 60

Met Trp Ala Thr Gly Glu Glu Leu Arg Lys Pro Pro Trp Gln Gly Ser 65 70 75 80

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- Tyr Tyr His Cys Asn Arg His His Trp Val Phe Gly Val Leu Leu Cys
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- Asn Val Val Thr Val Ala Phe Tyr Ala Asn Met Tyr Ser Ser Ile Leu 100 105 110
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- Thr Val Ala Cys Tyr Thr Ala Thr Ile Leu Lys Leu Leu Arg Thr Glu 210 215 220
- Glu Ala His Gly Arg Glu Gln Arg Arg Ala Val Gly Leu Ala Ala 225 230 235 240
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- His Val Tyr Lys Leu Thr Leu Cys Leu Ser Cys Leu Asn Asn Cys Leu

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Tyr Lys Gln Leu Glu Asp Ala Ala Gln Gly Leu Thr Met Gly Gly Asp 50 55 60

Val Glu Glu His Glu Asp Leu Thr Ala Asp Ser Thr Ile Phe Lys Phe 65 70 75 80

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Phe Leu Met 450	Ser Glu	Ala Val 455		Pro	Val	Thr	Pro 460	Glu	Pro	Cys	Val
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Ala Lys Asp	Thr Leu 485	Tyr His	Val	Leu	Tyr 490	Ile	Gly	Thr	Glu	Ser 495	Gly
Thr Ile Leu	Lys Ala 500	Leu Ser	Thr	Ala 505	Ser	Arg	Ser	Leu	His 510	Gly	Cys
Tyr Leu Glu 515	Glu Leu	His Val	Leu 520	Pro	Pro	Gly	Arg	Arg 525	Glu	Pro	Leu
Arg Ser Leu 530	Arg Ile	Leu His		Ala	Arg	Ala	Leu 540	Phe	Val	Gly	Leu
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Ser Gln Gly Ala Cys Leu Gly Ala Arg Asp Pro Tyr Cys Gly Trp Asp

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Gly Lys Gln Gln Arg Cys Ser Thr Leu Glu Asp Ser Ser Asn Met Ser 585 Leu Trp Thr Gln Asn Ile Thr Ala Cys Pro Val Arg Asn Val Thr Arg Asp Gly Gly Phe Gly Pro Trp Ser Pro Trp Gln Pro Cys Glu His Leu Asp Gly Asp Asn Ser Gly Ser Cys Leu Cys Arg Ala Arg Ser Cys Asp Ser Pro Arg Pro Arg Cys Gly Gly Leu Asp Cys Leu Gly Pro Ala Ile His Ile Ala Asn Cys Ser Arg Asn Gly Ala Trp Thr Pro Trp Ser Ser Trp Ala Leu Cys Ser Thr Ser Cys Gly Ile Gly Phe Gln Val Arg Gln Arg Ser Cys Ser Asn Pro Ala Pro Arg His Gly Gly Arg Ile Cys Val Gly Lys Ser Arg Glu Glu Arg Phe Cys Asn Glu Asn Thr Pro Cys Pro Val Pro Ile Phe Trp Ala Ser Trp Gly Ser Trp Ser Lys Cys Ser Ser Asn Cys Gly Gly Met Gln Ser Arg Arg Arg Ala Cys Glu Asn Gly Asn Ser Cys Leu Gly Cys Gly Val Glu Phe Lys Thr Cys Asn Pro Glu 760

Gly Cys Pro Glu Val Arg Arg Asn Thr Pro Trp Thr Pro Trp Leu Pro 770 775 780

Val Asn Val Thr Gln Gly Gly Ala Arg Gln Glu Gln Arg Phe Arg Phe 785 790 795 800

Thr Cys Arg Ala Pro Leu Ala Asp Pro His Gly Leu Gln Phe Gly Arg 805 810 815 Arg Arg Thr Glu Thr Arg Thr Cys Pro Ala Asp Gly Ser Gly Ser Cys 820 825 830

Asp Thr Asp Ala Leu Val Glu Val Leu Leu Arg Ser Gly Ser Thr Ser 835 840 845

Pro His Thr Val Ser Gly Gly Trp Ala Ala Trp Gly Pro Trp Ser Ser 850 855 860

Cys Ser Arg Asp Cys Glu Leu Gly Phe Arg Val Arg Lys Arg Thr Cys 865 870 875 880

Thr Asn Pro Glu Pro Arg Asn Gly Gly Leu Pro Cys Val Gly Asp Ala 885 890 895

Ala Glu Tyr Gln Asp Cys Asn Pro Gln Ala Cys Pro Val Arg Gly Ala 900 905 910

Trp Ser Cys Trp Thr Ser Trp Ser Pro Cys Ser Ala Ser Cys Gly Gly 915 920 925

Gly His Tyr Gln Arg Thr Arg Ser Cys Thr Ser Pro Ala Pro Ser Pro 930 935 940

Gly Glu Asp Ile Cys Leu Gly Leu His Thr Glu Glu Ala Leu Cys Ala 945 950 955 960

Thr Gln Ala Cys Pro Glu Gly Trp Ser Pro Trp Ser Glu Trp Ser Lys 965 970 975

Cys Thr Asp Asp Gly Ala Gln Ser Arg Ser Arg His Cys Glu Glu Leu 980 985 990

Leu Pro Gly Ser Ser Ala Cys Ala Gly Asn Ser Ser Gln Ser Arg Pro 995 1000 1005

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